PCT/EP 99 / 06423

The Patent Office

REC'D 14 OCT 1999

WIPO PCT

INVESTOR IN PEOPLE

EP 99/06423

The Patent Office
Concept House
Cardiff Road
Newport
South Wales
NP10 8QQ

PRIORITY DOCUMENT

SUBMITTED OR TRANSMITTED IN COMPLIANCE WITH RULE 17.1(a) OR (b)

I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

In accordance with the rules, the words "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

Re-registration under the Companies Act does not constitute a new legal entity but merely subjects the company to certain additional company law rules.

Signed P. Mahoney

Dated 3 August 1999

For Official use

THE PATENT OFFICE
C
-9 SEP 1998
RECEIVED BY POST

09SEP98 E388689-1 D02029
P01/7700 25.00 - 9819530.8

Your Reference: C70366

Notes
Please type, or write in dark ink using CAPITAL letters. A prescribed fee is payable for a request for grant of a patent. For details, please contact the Patent Office (telephone 071-483 4700).

Rule 16 of the Patents Rules 1990 is the main rule governing the completion and filing of this form.

❷ Do not give trading styles, for example, 'Trading as XYZ company', nationality or former names, for example, 'formerly (known as) ABC Ltd' as these are not required.

Warning
After an application for a Patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977 and will inform the applicant if such prohibition or restriction is necessary. Applicants resident in the United Kingdom are also reminded that under Section 23, applications may not be filed abroad without written permission unless an application has been filed not less than 6 weeks previously in the United Kingdom for a patent for the same invention and either no direction prohibiting publication or communication has been given, or any such direction revoked.

The Patent Office

Request for grant of a Patent

Form 1/77 **Patents Act 1977**

19 SEP

❶ Title of invention

1 Please give the title of the invention: NOVEL COMPOSITIONS AND USE

❷ Applicant's detail

First or only applicar **9819530.8**

2a If you are applying as a corporate body please give:

Corporate Name: SmithKline Beecham p.l.c.

Country *(and State of incorporation, if appropriate)*: United Kingdom

2b If you are applying as an individual or one of a partnership please give in full:

Surname

Forenames

2c **In all cases, please given the following details:**

Address: New Horizons Court, Brentford, Middlesex

UK postcode *(if applicable)*: TW8 9EP

Country: United Kingdom

ADP number *(if known)*: **5800974002**

2d, 2e and 2f: If there are further applicants please provide details on a separate sheet of paper

☐ **Second applicant *(if any)***

2d If you are applying as a corporate body please give:
Corporate Name

Country *(and State of Incorporation, if appropriate)*

2e If you are applying as an individual or one of a partnership please give in full:

Surname:

Forenames:

2f **In all cases,** please give the following details:

Address:

UK postcode
(if applicable)
Country
ADP number
(if known)

❸ *An address for service in the United Kingdom must be supplied*

Please mark correct box.

❸ **Address for service details**

3a Have you appointed an agent to deal with your application?

Yes ☒ No ☐ ➲ *go to 3b*

❶

please give details below

Agent's name	S M White
Agent's address	SmithKline Beecham Corporate Intellectual Property New Horizons Court. Bldg 2. Great West Road Brentford, Middlesex
Postcode	TW8 9EP
Agent's ADP number	

3b: *If you have appointed an agent, all correspondence concerning your application will be sent to the agent's United Kingdom address.*

3b If you have not appointed an agent please give a name and address in the United Kingdom to which all correspondence will be sent:

Name

Address

Postcode
number
ADP number
(if known)

Daytime telephone
(if available)

❹ Reference number

4. Agent's or applicant's reference number *(if applicable)* SMW/AC/C70366

❺ Claiming an earlier application date

5. Are you claiming that this application be treated as having been filed on the date of filing of an earlier application?

Please mark correct box

Yes ☐ No ☒ ➲ *go to 6*

❶ ***please give details below***

☐ number of earlier application or patent number

☐ filing date *(day month year)*

☐ and the Section of the Patents Act 1977 under which you are claiming:

Please mark correct box

15(4) (Divisional) ☐ 8(3) ☐ 12(6) ☐ 37(4) ☐

❻ Declaration of priority

6. If you are declaring priority from previous application(s), please give:

❻ *If you are declaring priority from a PCT Application please enter 'PCT' as the country and enter the country code (for example, GB) as part of the application number*

Please give the date in all number format, for example, 31/05/90 for 31 May 1990

Country of Filing	Priority application number *(if known)*	Filing Date *(day, month, year)*

❼ Inventorship

•any applicant is not an inventor
•there is an inventor who is not
•an applicant, or
•any applicant is a corporate body.

7. Are you (the applicant or applicants) the sole inventor or the joint inventors?
Please mark correct box

Yes ☐ No ☒ ➲ *A Statement of Inventorship on Patents form 7/77 will need to be filed (see Rule 15).*

❽ Checklist

❽ Please supply duplicates of claim(s), abstract, description and drawings).

8a Please fill in the number of sheets for each of the following types of document contained in this application

Continuation sheets for this Patents Form 1/77	–
Claim(s)	
Description	6
Abstract	
Drawing(s)	

8b Which of the following documents also accompanies the application?

Please mark correct box(es)

Priority documents *(please state how many)*	–
Translation(s) of Priority documents *(please state how many)*	–
Patents Form 7/77 - Statement of Inventorship and Right to Grant	–
Patents Form 9/77 - Preliminary Examination Report	–
Patents Form 10/77 - Request for Substantive Examination	–

❾ Request

❾ You or your appointed agent (see Rule 90 of the Patents Rules 1990) must sign this request.

I/We request the grant of a patent on the basis of this application.

Signed _____ Date: 08/09/98
(day month year)

Please sign here ✍

S M White
Chartered Patent Attorney
Attorney for the Applicant

A completed fee sheet should preferably accompany the fee.

Please return the completed form, attachments and duplicates where requested, together with the prescribed fee to either;

☑ *The Comptroller*	☐ *The Comptroller*
The Patent Office	*The Patent Office*
Cardiff Road	*25 Southampton Buildings*
Newport	*London*
Gwent	*WC2A 1AY*
NP9 1RH	

C70366

NOVEL COMPOSITION AND USE

The present invention relates to the use of thickening agents and stabilisers in acidic compositions for oral use such as foodstuffs and oral healthcare compositions to alleviate or prevent the tooth damage associated with the consumption of acid, namely dental erosion.

Dental erosion describes the "pathologic, chronic, localised, painless loss of dental hard tissue chemically etched away from the tooth surface by acid and/or chelation without bacterial involvement" (Imfeld, 1996). The acids causing the erosion are derived from dietary, occupational or intrinsic sources and are not products of the intraoral flora. With the trend towards an increase in eating and drinking frequency amongst all age groups it is likely that the incidence of dental erosion will increase.

International Patent Pubication (WO 97/30601) describes acid-based liquid compositions having reduced tooth erosion properties in which calcium is present in the range of 0.3 to 0.8 mol per mol of acid and which have a pH in the range 3.5 to 4.5.

Complex polysaccharide gums are routinely added to beverages and other foodstuffs as thickeners, stabilisers and texturisers. These include alginates, locust bean gum, gellan gum, guar gum, gum arabic, xanthan gum, pectates, cellulose derivatives (e.g. carboxymethyl cellulose) and other thickeners known in the art.

Van der Reijden et al (Caries Res., 1997, 31, 216-23) describes the protective effect of saliva substitute compositions containing thickening agents on demineralisation of enamel *in vitro*. A pH cycling experiment is described in which bovine enamel is exposed to demineralisation buffer (pH 4.8) and remineralisation buffer (pH 7.0) containing a range of dissolved polymers.

It has now been found that the addition of stabilizers and thickeners to acidic foodstuffs and oral healthcare compositions reduces tooth erosion due to the loss of calcium and phosphate from tooth enamel generally associated with such products.

Furthermore, it has surprisingly been found that addition of a complex polysaccharide and calcium to an acidic composition for oral use reduces the loss of calcium and phosphate from tooth enamel to a greater extent than is conferred by addition of either complex polysaccharide or calcium alone.

Accordingly, the present invention provides the use of a complex polysaccharide material as a tooth erosion inhibitor in an acidic composition for oral administration wherein the effective pH of the composition is less than or equal to 4.5.

In a further aspect the invention provides a composition for oral use comprising an acidulant, a complex polysaccharide gum and calcium wherein calcium is present in an amount up to 0.8 mol per mol of acid and the effective pH of the composition is less than or equal to 4.5.

Suitably compositions for use in the invention will have an effective pH in the range 2.5 to 4.5, more suitably from 2.8 to 4.0.

Suitable complex polysaccharide materials for use in compositions of the invention include stabilisers and thickening agents such as alginates, locust bean gum, gellan gum, guar gum, gum arabic, xanthan gum, pectates, cellulose derivatives (e.g. carboxymethyl cellulose) and other such materials used in the field of foodstuffs and other compositions for oral use, including mixtures of one or more thereof.

The invention is applicable to all acidic products for oral consumption or use. These include acidic beverages, vinegars, sauces, pickles, preserves, confectionery and diverse acidic products such as acidic dairy products, and also to other substances, suitably in liquid form, to be taken orally such as acidic mouth washes and medicines.

The invention may be applied to a variety of solid, semi-solid or liquid foodstuffs, particularly acidic beverages. These include still fruit drinks, carbonated soft drinks and in particular health drinks such as blackcurrant juice drinks or vitamin added beverages. The invention also extends to concentrates and powdered forms for preparing acidic beverages.

The invention is advantageously applied to acidic compositions, in particular foodstuffs and especially beverages, containing natural or added acidulants. The acid composition may contain organic and/or inorganic acids and may be supplemented with vitamins such as ascorbic acid. Preferred acidulants include potable acids such as citric, malic, lactic, phosphoric and tartaric acids and mixtures thereof.

Foodstuffs such as beverages may be unsweetened or sweetened with natural sugars or synthetic sweeteners such as saccharine, aspartyl phenyl alanyl methyl ester, or other sweeteners known in the art. Compositions may also contain other conventional additives such as sodium benzoate, sorbic acid, sodium metabisulfite, ascorbic acid, flavourings, colourings and carbon dioxide.

The term effective pH is used in the context of the present invention to mean the pH of the composition when in liquid form or the pH of the composition before solidification (where the composition is a solid or semi-solid prepared via a liquid phase intermediate) or the pH of a solid or semi-solid composition when reconstituted or dissolved in a liquid, eg. water. The term solidification encompasses the treatment or supplementation of liquid phase intermediates to form a solid or semi-solid.

A further advantage arises from the use of low levels of calcium, suitably in the form of an alkaline salt. When calcium is present, the buffering capacity of the formulation is reduced by partial neutalisation of the acid, which allows saliva to neutralise remaining acid residues in the mouth more rapidly.

When calcium is present, the absolute concentration is not critical as this will vary according to the nature and concentration of the acids present. Calcium may be added in any suitable form, conveniently as a soluble salt such as calcium carbonate, calcium hydroxide, calcium citrate, calcium malate, calcium lactate, calcium chloride, calcium glycerophosphate or calcium formate or any other salt which minimises any adverse flavour contribution to the composition. The molar ratio of calcium to acid may be from 0.05 to 0.75, typically 0.1 to 0.5.

In a further aspect, the present invention provides a method of reducing the tooth erosion potential of an acidic composition for oral use comprising adding a complex polysaccharide material, and optionally calcium in the range 0 to 0.8 mol per mol of acid, to an acidic oral composition and, if necessary or desired, controlling the effective pH so that it is less than or equal to 4.5.

For the avoidance of doubt, the phrase 'if necessary or desired' encompasses control of pH to bring it into the defined range as well as control of pH within the defined range. The effective pH of the formulation may be adjusted to the desired value by the addition of alkali, eg. a soluble alkaline salt such as sodium hydroxide or sodium citrate, sodium malate or sodium lactate and by the addition of calcium when present.

The invention also extends to a method of reducing tooth erosion caused by acid in orally administered compositions comprising orally administering a composition comprising a complex polysaccharide and an acidulant, and optionally containing calcium in the range 0 to 0.8 mol per mol or acid, wherein the effective pH of the composition is less than or equal to 4.5.

The invention further extends to the use of a composition comprising a complex polysaccharide and an acidulant having a pH less than or equal to 4.5, optionally containing calcium in the range 0 to 0.8 mol per mol of acid, in the manufacture of a medicament for the reduction of tooth erosion caused by acid in orally administered compositions.

Typically the acid concentration in compositions of the invention, for example the citric acid or malic acid concentration in a fruit-based product would be in the range 0.01% w/w to 4% w/w, suitably in the range 0.1% w/w to 2.5% w/w. Mixtures of potable acids may be used, for example mixtures of acids selected from citric, malic, phosphoric and lactic acids and other suitable food grade excipients known in the art.

Oral compositions may contain magnesium or other ions as adjuncts for

remineralisation. They may also contain an effective amount of malic acid or potable salts thereof to maintain the solubility of calcium, when present, so as to prevent or minimize the precipitation of insoluble calcium salts. Added malic acid may provide as little as 10% of the total acidity of the beverage, the remainder of the acidity being provided by other, preferably naturally present, acids such as citric acid, or by ascorbic acid.

Oral compositions may be prepared by mixing the ingredients according to conventional methods. Solid ingredients may be dissolved in water or in hot water if required prior to addition to other components. Complex polysaccharides are generally hydrated in water with high shear mixing before addition. Typically beverages and other liquid products are pasteurised prior to filling in bottles or cans or other packs or are "in-pack pasteurised" after filling.

The following examples are illustrative of the invention.

Example 1

1000L of a ready to drink beverage (pH 3.5) was prepared by mixing ingredients as follows:

Ingredients	Quantity
Orange juice	110L
Citric Acid	3.8Kg
Acesulfame K	0.74Kg
Aspartame	0.72Kg
Ascorbic Acid	0.29Kg
Orange Flavouring	0.4L
Xanthan Gum (Keltrol T) (Nutrasweet Kelco, Tadworth, England)	0.34Kg
Water to 1000L	

A control beverage was prepared without the addition of xanthan gum. The two beverages were tested for their potential to dissolve enamel in an *in vitro* protocol in which flat dental enamel sections were exposed to test solutions at a temperature of 37°C for 4 hours. Erosive potential was evaluated by physical measurement of the depth of enamel lost during the procedure. The control beverage without the thickening agent gave an enamel loss of 16 μm over the 4 hour exposure period as compared to the beverage with xanthan gum which gave an enamel loss of 1 μm.

Example 2

1000Kg of a powdered orange sports drink was prepared by mixing the following ingredients:

Ingredient	Quantity (Kg)
Dextrose monohydrate	400
Maltodextrin	538
Aspartame	0.6
Acesulfame k	0.38
Sodium citrate	17.0
Citric acid	38.0
Ascorbic acid	1.2
Potassium citrate	2.4
Vitamin Premix (B2, B6, B12, Niacin, Pantothenic acid)	0.4
Orange flavour	3.0
Beta-Carotene (1%)	6.0
Blanose Cellulose Gum (9M31XF) (Hercules Limited, Reigate, England)	1.0

A beverage (pH 3.4) is prepared for consumption by dilution of the powder (50g) in water (500mL).

Example 3

Solutions of citric acid were prepared in deionised water and adjusted to pH 3.8 with 0.1M sodium hydroxide solution. Calcium was added in the form of calcium carbonate and/or xanthan gum was added as Keltrol T (Nutrasweet Kelco Co. Ltd., Tadworth, Surrey). All solutions were tested in a 4 hour *in vitro* protocol as described in Example 1.

Results

Citric Acid Monohydrate (CAMH) (%w/v)	Xanthan Gum (%w/v)	Ca/CAMH Mol Ratio	4hr Enamel Loss (μm)
0.3	**0**	**0**	**7.6**
0.3	**0.034**	**0**	**5.3**
0.3	**0**	**0.3**	**5.4**
0.3	**0.034**	**0.3**	**2.8**

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☑ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☑ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.
As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.